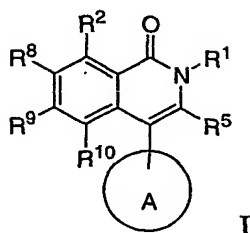


WHAT IS CLAIMED IS:

1. A compound of the structure:



- 5 or a pharmaceutically acceptable salt, crystal form, or hydrate, wherein:

A is

a) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with

- 1) halogen,
- 2) NO₂,
- 3) CN,
- 4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,
- 5) C≡C R⁴⁶,
- 6) (CRⁱR^j)_rOR⁴⁶,
- 7) (CRⁱR^j)_rN(R⁴⁶R⁴⁷),
- 8) (CRⁱR^j)_rC(O)R⁴⁶,
- 9) (CRⁱR^j)_rC(O)OR⁴⁶,
- 10) (CRⁱR^j)_rR⁴⁶,
- 11) (CRⁱR^j)_rS(O)₀₋₂R⁶¹,
- 12) (CRⁱR^j)_rS(O)₀₋₂N(R⁴⁶R⁴⁷),
- 13) OS(O)₀₋₂R⁶¹,
- 14) N(R⁴⁶)C(O)R⁴⁷,
- 15) N(R⁴⁶)S(O)₀₋₂R⁶¹,
- 16) (CRⁱR^j)_rN(R⁴⁶)R⁶¹,
- 17) (CRⁱR^j)_rN(R⁴⁶)R⁶¹OR⁴⁷,
- 18) (CRⁱR^j)_rN(R⁴⁶)(CR^kR^l)_sC(O)N(R⁴⁷R⁴⁸),
- 19) N(R⁴⁶)(CRⁱR^j)_rR⁶¹,
- 20) N(R⁴⁶)(CRⁱR^j)_rN(R⁴⁷R⁴⁸),
- 21) (CRⁱR^j)_rC(O)N(R⁴⁷R⁴⁸), or

22) oxo, or

b) a heteroaryl ring selected from the group consisting of

a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and

a 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or substituted with

1) halogen,

2) NO₂,

3) CN,

4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,

5) C≡CR⁴⁶,

6) (CRⁱR^j)_TOR⁴⁶,

7) (CRⁱR^j)_TN(R⁴⁶R⁴⁷),

8) (CRⁱR^j)_T C(O)R⁴⁶,

9) (CRⁱR^j)_T C(O)OR⁴⁶,

10) (CRⁱR^j)_TR⁴⁶,

11) (CRⁱR^j)_T S(O)₀₋₂R⁶¹,

12) (CRⁱR^j)_T S(O)₀₋₂N(R⁴⁶R⁴⁷),

13) OS(O)₀₋₂R⁶¹,

14) N(R⁴⁶)C(O)R⁴⁷,

15) N(R⁴⁶)S(O)₀₋₂R⁶¹,

16) (CRⁱR^j)_TN(R⁴⁶)R⁶¹,

17) (CRⁱR^j)_TN(R⁴⁶)R⁶¹OR⁴⁷,

18) (CRⁱR^j)_TN(R⁴⁶)(CR^kR^l)_SC(O)N(R⁴⁷R⁴⁸),

19) N(R⁴⁶)(CRⁱR^j)_TR⁶¹,

20) N(R⁴⁶)(CRⁱR^j)_TN(R⁴⁷R⁴⁸),

21) (CRⁱR^j)_TC(O)N(R⁴⁷R⁴⁸), or

22) oxo;

R¹ is selected from the group consisting of

- 1) hydrogen,
- 2) (CR^aR^b)_nR⁴⁰
- 3) (CR^aR^b)_nOR⁴⁰,
- 4) (CR^aR^b)_nN(R⁴⁰R⁴¹),
- 5) (CR^aR^b)_nN(R⁴⁰)C(O)OR⁴¹,
- 6) (CR^aR^b)_nN(R⁴⁰)(CR^cR^d)₂N(R⁴¹)C(O)R⁴⁹,
- 7) C₃₋₈ cycloalkyl,
- 8) (CR^aR^b)_nC(O)OR⁴⁰,
- 9) (CR^aR^b)_nN(R⁴⁰)(CR^cR^d)₁₋₃R⁴¹,
- 10) (CR^aR^b)_nS(O)₀₋₂R⁶,
- 11) (CR^aR^b)_nS(O)₀₋₂N(R⁴⁰R⁴¹),
- 12) (CR^aR^b)_nN(R⁴⁰)R⁶OR⁴¹,
- 13) (CR^aR^b)_nN(R⁴⁰)(CR^cR^d)₀₋₆C(O)N(R⁴¹R⁴²);

R⁵ is selected from the group consisting of

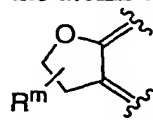
- 1) C(O)N(R⁵⁵R⁵⁰),
- 2) C(O)OR⁵⁵, and
- 3) C(O)R⁸²;

R², R⁸, R⁹ and R¹⁰ are independently selected from:

- 1) hydrogen,
- 2) halogen,
- 3) NO₂,
- 4) CN,
- 5) CR⁴³=C(R⁴⁴R⁴⁵),
- 6) C≡CR⁴³,
- 7) (CR^eR^f)_pOR⁴³,
- 8) (CR^eR^f)_pN(R⁴³R⁴⁴),
- 9) (CR^eR^f)_pC(O)R⁴³,
- 10) (CR^eR^f)_pC(O)OR⁴³,
- 11) (CR^eR^f)_pR⁴³,
- 12) (CR^eR^f)_pS(O)₀₋₂R⁶⁰,
- 13) (CR^eR^f)_pS(O)₀₋₂N(R⁴³R⁴⁴),
- 14) OS(O)₀₋₂R⁶⁰,
- 15) N(R⁴³)C(O)R⁴⁴,

- 16) $N(R^{43})S(O)_{0-2}R^{60}$,
 17) $(CReRf)_pN(R^{43})R^{60}$,
 18) $(CReRf)_pN(R^{43})R^{60}OR^{44}$,
 19) $(CReRf)_pN(R^{43})(CReRh)_qC(O)N(R^{44}R^{45})$,
 20) $N(R^{43})(CReRf)_pR^{60}$,
 21) $N(R^{43})(CReRf)_pN(R^{44}R^{45})$, and
 22) $(CReRf)_pC(O)N(R^{43}R^{44})$,

or R^2 and R^8 are independently as defined above, and R^9 and R^{10} , together with the atoms to which they are attached, form the ring



, where R^m is C_{1-6} alkyl;

$R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, R^i, R^j, R^k$ and R^l are independently selected from the group consisting of:

- 1) hydrogen,
- 2) C_1-C_6 alkyl,
- 3) halogen,
- 4) aryl,
- 5) R^{80} ,
- 6) C_3-C_{10} cycloalkyl, and
- 7) OR^4 ,

said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with R^7 , disubstituted with R^7 and R^{15} , trisubstituted with R^7 , R^{15} and R^{16} , or tetrasubstituted with R^7 , R^{15} , R^{16} and R^{17} ;

$R^4, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, R^{46}, R^{47}, R^{48}, R^{49}, R^{50}, R^{51}, R^{52}$, and R^{55} are independently selected from the group consisting of

- 1) hydrogen,
- 2) C_1-C_6 alkyl,
- 3) C_3-C_{10} cycloalkyl,
- 4) aryl,
- 5) R^{81} ,
- 6) CF_3 ,
- 7) C_2-C_6 alkenyl, and
- 8) C_2-C_6 alkynyl,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R¹⁸, di-substituted with R¹⁸ and R¹⁹, tri-substituted with R¹⁸, R¹⁹ and R²⁰, or tetra-substituted with R¹⁸, R¹⁹, R²⁰ and R²¹;

5 R⁶, R⁶⁰, R⁶¹, and R⁶² are independently selected from the group consisting of

- 1) C₁-C₆ alkyl,
- 2) aryl,
- 3) R⁸³, and
- 4) C₃-C₁₀ cycloalkyl;

10 said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R²⁶, di-substituted with R²⁶ and R²⁷, tri-substituted with R²⁶, R²⁷ and R²⁸, or tetra-substituted with R²⁶, R²⁷, R²⁸ and R²⁹;

R⁷, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²⁶, R²⁷, R²⁸, and R²⁹ are independently selected from the group consisting of

- 15 1) C₁-C₆ alkyl,
- 2) halogen,
- 3) OR⁵¹,
- 4) CF₃,
- 5) aryl,
- 20 6) C₃-C₁₀ cycloalkyl,
- 7) R⁸⁴,
- 8) S(O)₀₋₂N(R⁵¹R⁵²),
- 9) C(O)OR⁵¹,
- 10) C(O)R⁵¹,
- 25 11) CN,
- 12) C(O)N(R⁵¹R⁵²),
- 13) N(R⁵¹)C(O)R⁵²,
- 14) S(O)₀₋₂R⁶²,
- 15) NO₂, and
- 30 16) N(R⁵¹R⁵²);

R⁸⁰, R⁸¹, R⁸², R⁸³, and R⁸⁴ are independently selected from a group of unsubstituted or substituted heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a

9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S; and

n, p, q, r, and s are independently 0, 1, 2, 3, 4, 5 or 6.

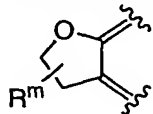
5 2. A compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein

A is an aryl ring selected from phenyl, unsubstituted or substituted as in Claim 1, or a heteroaryl ring, unsubstituted or substituted as in Claim 1, selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, indole, pyrrolopyridine, benzimidazole, benzoxazole, benzothiazole, and benzoxadiazole;

10 R², R⁸, R⁹ and R¹⁰ are independently selected from the group consisting of:

- 1) hydrogen,
- 2) halogen,
- 3) OR⁴³, and
- 15 4) (CR^eR^f)_pR⁴³,

or R² and R⁸ are independently as defined above, and R⁹ and R¹⁰, together with the atoms to which they are attached, form the ring



, where R^m is C₁₋₆alkyl;

R¹ is selected from the group consisting of

- 20 1) hydrogen,
- 2) (CR^aR^b)₁₋₂R⁴⁰
- 3) (CR^aR^b)₁₋₂OR⁴⁰,
- 4) (CR^aR^b)₁₋₂N(R⁴⁰R⁴¹),
- 5) (CR^aR^b)₁₋₂N(R⁴⁰)C(O)OR⁴¹,
- 25 6) (CR^aR^b)₁₋₂N(R⁴⁰)(CR^cR^d)₂N(R⁴¹)C(O)R⁴⁹,
- 7) (CR^aR^b)₁₋₂C(O)OR⁴⁰,
- 8) (CR^aR^b)₁₋₂N(R⁴⁰)(CR^cR^d)₁₋₃R⁴¹, and
- 9) cyclopropyl.

30 3. A compound of Claim 2, or a pharmaceutically acceptable salt thereof, wherein

R², R⁸, R⁹ and R¹⁰ are independently selected from the group consisting of

- 1) hydrogen,
- 2) halogen, and
- 3) (C^eR^f)_pOR⁴³.

5

4. A compound of Claim 3, or a pharmaceutically acceptable salt thereof,

wherein

R¹ is selected from the group consisting of

- 1) hydrogen,
- 2) (C^aR^b)_nR⁴⁰, and
- 3) (C^aR^b)_nOR⁴⁰.

10

5. A compound of Claim 4, or a pharmaceutically acceptable salt thereof,

wherein

15 A is an aryl ring, wherein the aryl ring atom is unsubstituted or substituted with halogen; and

R⁵ is selected from the group consisting of

- 1) C(O)N(R⁵⁵R⁵⁰),
- 2) C(O)OR⁵⁵, and
- 3) C(O)R⁸².

20

6. A compound of Claim 5, or a pharmaceutically acceptable salt thereof,

wherein

R¹ is -CH₃, -CH₂CHCH₂, or cyclopropyl;

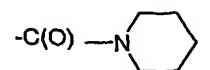
R² and R¹⁰ are hydrogen;

25 R⁸ is hydrogen or -OCH₃;

R⁹ is hydrogen or -OCH₃; and

R⁵ is selected from the group consisting of

-C(O)N(CH₃)₂, -C(O)NH₂, -C(O)OCH₃, -C(O)OH, -C(O)OCH₂CH₃, and



30

7. A compound of Claim 6, or a pharmaceutically acceptable salt thereof, selected from the group consisting of

4-(3-fluorophenyl)-6-methoxy-n,n,2-trimethyl-1-oxo-1,2-dihydroisoquinoline-3-carboxamide,

4-(3-fluorophenyl)-6-methoxy-2-methyl-3-(pyrrolidin-1-ylcarbonyl)isoquinolin-1(2H)-one,

2-allyl-6-methoxy-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxamide,

6-methoxy-2-methyl-4-phenyl-3-pyridin-2-ylisoquinolin-1(2h)-one,

2-cyclopropyl-6-methoxy-4-phenyl-3-(1,3-thiazol-2-yl)isoquinolin-1(2h)-one,

methyl 4-(3-fluorophenyl)-6-methoxy-2-methyl-1-oxo-1,2-dihydroisoquinoline-3-carboxylate,

methyl 6-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate,

7-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylic acid,

methyl 7-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate, and

ethyl 2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate.

5 8. A method of treating a condition in a mammal, the treatment of which is effected or facilitated by K_v1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting K_v1.5.

9. A method of Claim 8, wherein the condition is cardiac arrhythmia.

10. A method of Claim 9, wherein the cardiac arrhythmia is atrial fibrillation.

11. A method of Claim 9, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

5 12. A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by $K_v1.5$ inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting $K_v1.5$.

13. A method of Claim 12, wherein the condition is cardiac arrhythmia.

10 14. A method of Claim 13, wherein the cardiac arrhythmia is atrial fibrillation.

15 15. A method of Claim 13, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

16. A method of Claim 12, wherein the condition is a thromboembolic event.

17. A method of Claim 16, wherein the thromboembolic event is a stroke.

20 18. A method of Claim 12, wherein the condition is congestive heart failure.

25 19. A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound Claim 1 or a pharmaceutically acceptable crystal form or hydrate thereof.

20. A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

30 21. A method of treating cardiac arrhythmia comprising administering a compound of Claim 1 with a compound selected from one of the classes of compounds consisting of antiarrhythmic agents having $K_v1.5$ blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta blockers, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs, warfarin, factor Xa inhibitors, low molecular weight
35 heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT

receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

22. A method for inducing a condition of normal sinus rhythm in a patient
5 having atrial fibrillation, which comprises treating the patient with a compound of Claim 1.

23. A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of Claim 1.